

Human A4 Receptor

1 TTGAGCCGGCAGACTGCGAAAACTAGCTGGAGCCGGAGCGGACAGAACTGTTGCTGTCAGACGGGCTTGTTGGTTCTCCCGCGGACAGGGCTCGCCGGGAGAGTTTCATC 120  
121 ATGAATGAGAAATGGGACACAAACTCTTTCAGAAAATGCGATCCCATCTGGAATGTCATGACACAAAGCATCATCTGTAATGATATATATATACCTATGTCGAACACTATCTTTCAC 240  
1 M N E K W D T N S S E N W H P I W N V N D T K H L Y S D I N I T Y V N Y Y L H 40  
241 CAGCCTCAAGTGGCAGCAATCTTCATTTATTTCTGATCTCTTTTCTGATCTCTTTTCTGATGATGGAAATACTGTGTTGCTTTTATTTAATGAGGAAACAAACATATGACACAGTCACT 360  
41 Q P Q V A A I F I I S Y F L I F L C M M G N T V V C F I V M R N K H M H T V T 80  
361 AATCTCTCTCTTAAACCTGGCCATAAGTCAATTTACTTACTAGTTGGCATATTTCTGCACTGTCGCAATATTAAGCAGGATGGCCATTTGGAAACACGATGTGCAAGATC 480  
81 N L F I L N L A I S D L L V G I F C M P I T L L D N I I A G W P F G N T M C K I 120  
481 AGTGGATTGTTCCAGGGAATATCTGTCGACCTTCAGTCTTTTACGTTAGTTGCAATGCTGTAGATAGGTTCCAGTGTGTTGCTTACCCCTTTTAAACCAAGTCACTATCAAGACAGCG 600  
121 S G L V Q G I S V A A S V F T L V A I A V D R F Q C V V Y P F K P K L T I K T A 160  
601 TTGTGATTTATATCATCATCTGGTCTCTAGCCATCACCATTTATGCTCCATCTGCAATGTCAGTAATGTCATGTCGCAAGAAATATTAACGAGTGAGACTCAACTCCACAGATAAAACC 720  
161 F V I I M I I W V L A I T I M S P S A V M L H V Q E E K Y Y R V R L N S Q N K T 200  
721 AGTCCAGTCTACTGGTGGCGGAAGACTGGCCAAATCAGGAATAGGAAGATCTACACACTGTGCTTTTGCAACATCTACCTGGCTCCCTCTCCCTCATTTGTCATCATGTATGGA 840  
201 S P V Y W C R E D W P N Q E M R K I Y T T V L F A N I Y L A P L S L I V I M Y G 240  
841 AGGATTGGAAATTTCACTCTTCAGGGCTGCAGTTCTCOTCACAGGCGAGGAACCCAGGAGCAGTGGCAGCGTGTGCCAGGAAGACAGAGATCATTTAAGATGCTCTGATTTGGGCC 960  
241 R I G I S L F R A A V P H T G R K N Q E Q W H V V S R K K I I K M L L I V A 280  
961 CTGCTTTTATCTCTCATGGCTGCCCTCTGGAATCTTAATGATGCTCTCAGACTACGCTGACCTTTCTCCAATGAAGTGCAGATCATCAACATCTACATCACTTTTGCACACTGG 1080  
281 L L F I L S W L P L W T L M M L S D Y A D L S P N E L Q I I N I Y I Y P F A H W 320  
1081 CTGGCATTCGGCAACAGCAGTGTCAATCCCATCATTTATGTTTCTTCAAGAGATTTCCGCGCTGGTTTCCAGAGCTTCCAGCTCCAGCTCGCQ L C Q K R A K P M 1200  
321 L A F G N S S V N P I I Y G F F N E N F R R G F Q E A F Q L Q L C Q K R A K P M 360  
1201 GAAGCTTATACCCCTAAAGCTAAAGCCATGTGCTCATATAACACATCTATCAGCTTGTCCAGGAATCTTACATTTCAAAACCCCTCATGGGAAACCTTTGCTTTATAGGAAAAGTCTGAA 1320  
361 E A Y T L K A K S H V L I N T S N Q L V Q E S T F Q N P H G E T L L Y R K S A E 400  
1321 AAACCCCAACAGGAATTTAGTGTGGAAGAAATTTAAAGAACTACTAAACAGCAGTGAATTTAAAGAGCTAGTGTGATAATCCCTAACTCTACTACGCATTATATTTAAATCCATTGC 1440  
401 K P Q Q E L V M E E L K E T T N S S E I \* 421

- TM1 47-69
- TM2 82-104
- TM3 121-141
- TM4 160-182
- TM5 218-240
- TM6 275-297
- TM7 312-336

Figure 1

## Amino Acid Homologies of A4 and Related Mammalian Receptors

Note: All sequences are human

Numbers below represent % similarity / % identity

A4	Orexin1	Orexin2	Y1	Y2	Y4	Y5	Gastrin	CCKA	NK1	Mu	
100	59/32	61/32	63/31	61/30	59/28	61/28	61/28	63/31	55/26	62/25	A4
	100		58/26	59/32	64/32	61/26	58/27	59/30	59/32	58/26	Orexin1
		100	60/27	60/31	63/32	59/26	61/29	58/29	56/31	58/28	Orexin2
			100	63/31	71/43	66/32	60/30	56/28	54/29	54/24	Y1
				100	62/33	63/32	56/27	56/29	59/30	57/24	Y2
					100	64/29	54/29	56/28	53/26	54/25	Y4
						100	58/28	55/26	57/24	61/26	Y5
							100	73/50	55/27	58/24	Gastrin
								100	57/30	55/26	CCKA
									100	60/26	NK1
										100	Mu

### Legend:

Code:	GenBank Assession No.	Description
Orexin 1	AF041243	Human Orexin receptor-1
Orexin2	AF041245	Human Orexin receptor-2
Y1	P25929	Human Neuropeptide receptor Type1
Y2	P49146	Human Neuropeptide receptor Type2
Y4	P50391	Human Neuropeptide receptor Type4
Y5	U56079	Human Neuropeptide receptor Type5
Gastrin	P32239	Human Gastrin/Cholecystokinin Type B receptor
CCKA	P32238	Human Cholecystokinin Type A receptor
NK1	P25103	Human Neurokinin-1 / Substance-P receptor
Mu	P35372	Human Mu-type opioid receptor

Data above was obtained using the GAP program from the WISCONSIN PACKAGE Version 9.0

Parameters used: Symbol comparison table: oldpep.cmp \*  
Gap Creation Penalty: 30  
Gap Extension Penalty: 1

\* This is the default scoring matrix used by versions of the Wisconsin Package prior to Version 9.0. based on hte PAM250 table from M. Dayhoff<sup>1</sup>.

1.) Schwartz, R. M. and Dayhoff, M. O. [1979]. Matrices for Detecting Distant Relationships. In *Atlas of Protein Sequence and Structure*, (M.O. Dayhoff, ed.), 5, Suppl. 3, (pp; 353-358), National Biomedical Research Foundation, Washington D.C., USA.

Figure 2

# A4 vs. Human Y1 receptor

Percent Similarity: 63.032

Percent Identity: 30.585

1 MNEKWDTNSSSENWHPINNV.NDTKHHLYSDINXTYVNYLHQPQVAAIFI 49  
 1 .....MNSTLFSQVENHSVHSNFSEKNAQLLAFENDDDCHLPLAMI 40  
 50 ISXFL....IFFLCMMGNTVVCFIVMRNKHMTVTNLFILNLAISDLLVG 95  
 41 FTLALAYGAVIILGVSGNLALIIILKQKEMRNVNLTIVNLSFSDLLVA 90  
 96 IFCMPITLLDNIAGWPFGNTMCKISGLVQGISVAASVFTLVIAIADRFO 145  
 91 IMCLPFTFVYTLMDHWVFGAMCKLNPFVQCVSITVSIFSLVLIIVERHQ 140  
 146 CVVYPFKPKLTIKTAFVIIMIIVWLAITIMSPSAVMLHVQEEKYYRVRLN 195  
 141 LIINPRGWRPNNRHAYVGVIAVIWVLAVASSLPFLIYQVMTDEPFQNVTL 190  
 196 SQNKTSVPVYWCREDWPNQEMRKIYTTVLFANIYLAFLSLIVIMYGRIGIS 245  
 191 AYKDK...YVCFDQFPDSHRLSYTTLTLLVLQYFGPLCFIFICYFKIYIR 237  
 246 LFRAAVPHTGRKNQEQWHVVSRRKQKIIMLLIVALLFILSWLPLWTLMM 295  
 238 LKRRNNMMDKMRDNKYR...SSETKRINIMLLSIVVAFVAVCWLPITIFNT 284  
 296 LSDYADLSPNELQIINIY...IYPFAHWLAFGNSSVNPIIYGFENENFR 341  
 285 VFDWNH.....QIIATCNHNLLPLLCHLTAMISTCVNPIFYGFLNKNFQ 328  
 342 RGFOEAFQLQLCQKRAKPMEAYTLKAKSHVLINTSNQLVQESTFQNPHE 391  
 329 RDLQ..FFNFCDFRSRD.DDYETIAMSTMHTDVSKTSLK.....QAS 368  
 392 TLLYRKSAEKPQOELVMEELKETNSSEI\* 421  
 369 PVAFKKINNNDNEKI\*..... 385

Figure 3

[illegible][illegible]

Figure 4

[illegible]

Percent Identity: 31.081

Figure 5

[illegible]

Figure 6